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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,653	04/03/2006	Jeffrey Michael Axten	P33070	6839

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EXAMINER	
HABTE, KAHSAY	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
12/18/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/518,653	AXTEN ET AL.	
	Examiner	Art Unit	
	Kahsay T. Habte	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-21 and 23-31* is/are pending in the application.

4a) Of the above claim(s) *28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21,23,25,26,30 and 31* is/are rejected.

7)☒ Claim(s) *24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 16-21 and 23-31 are pending in this application.

Election/Restrictions

2. Applicant's election with of Group III (R^5_2 = 2,3-dihydro-[1,4]dioxino[2,3-c]pyridine in the reply filed on 11/26/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
Claims 28-29 are withdrawn from prosecution as being drawn to non-elected inventions.

3. The claims are drawn to multiple inventions for reasons set forth in the restriction requirement. The claims are examined only to the extent that they read on the elected invention. Cancellation of the non-elected subject matter is recommended in response to this Office Action. Applicants have to replace R5 with the core structure (i.e. 2,3-dihydro-[1,4]dioxino[2,3-c]pyridine) shown in Examples 37-39 and 41-42. Applicants are permitted substitution on the 2,3-dihydro-[1,4]dioxino[2,3-c]pyridine ring according to the specification. Note that the definition of R4 "containing up to four heteroatoms" and the definition of Y1 and Y2 do not limit the invention to Group III. Please see the 112 second paragraph rejections in the related case 11/814,610.

Information Disclosure Statement

4. Applicant's Information Disclosure Statement, filed on 12/16/2005 has been acknowledged. Please refer to Applicant's copies of the 1449 submitted herewith.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a bacterial infection due to Gram-positive organisms selected from *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes, Enterococcus faecalis, Enterococcus faecium*; and Gram-negative organisms selected from *Haemophilus influenza*, *E. Coli*, and *Moraxella catarrhalis Ravasio* (based on the antimicrobial activity provided in page 97), does not reasonably provide enablement for a method of treating bacterial infections generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence

or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to 'a method of treating bacterial infections' - which covers all types of bacteria and the infections due to them, without any particular cause, that are known to exist and those that may be discovered in the future, for which there is no enablement provided. There are no test procedures/assays provided to test the pharmaceutical or therapeutic activity of the compounds or efficacy in treating 'any disease or disorder due to bacterial infection' in general and none of the compounds have been tested to cover the effectiveness for all types of infections due to the bacterial and diseases or disorders due to bacterial infections generally. The test procedures provided in the specification in page 97 are specifically drawn to test the efficacy of the compounds to against specific Gram-positive and Gram-negative organisms, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to treatment or controlling of **all** types of bacterial infections and diseases or disorders embraced the instant claims. One of ordinary skill would not know to extrapolate this test data to method of treating diseases or disorders generally. Further, there is no reasonable basis for assuming that all the compounds embraced by the claims will share the same physiological properties and will be useful generally against any type of disease because there is no basis in the prior art for assuming the same.

Also see MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area. It is inconceivable as to how the claimed compounds can treat all types of diseases. For example, there is no known common therapeutic mechanism for all types of diseases generally. For example, there are more than 400 distinct viruses that infect humans producing a wide range of diseases. Bacterial infections are caused by the presence and growth of microorganisms that damage host tissue. The extent of infection is generally determined by how many organisms are present and the toxins they release. Infectious diseases are human illnesses caused by viruses, bacteria, parasites, fungi and other microbes. They may be spread by direct contact with an infected person or animal, by ingesting contaminated food or water, by insects like mosquitoes or ticks (disease vectors), or by contact with contaminated surroundings like animal droppings or even contaminated air. Bacteria can cause a range of different problems in different parts of the body. Applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of preventing solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Snyder et al., *J. Med. Liban* 48(4): 208-214, 2000 (PubMed Abstract provided), wherein with regards to antibacterial therapies, it is stated that “common bacteria whose susceptibility to antimicrobials is no longer predictable”.

Note also that despite the fact there are several commercial antibacterial agents are available, it is still difficult to treat several pathogens such as those cause leprosy, meningitis, sexually transmitted infections, anthrax etc.

No compound has ever been found that can **control** or treat bacterial infections generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. Nearly all drugs for treating infections are effective against only a limited group of disorders. Therefore, a compound effective against disorders of the neuronal system generally would be a revolutionary exception. It is well established that an enablement rejection is proper when the scope of enablement is not reasonably correlated to the scope of the claims. (*In re Vaeck*, 20 USPQ2d 1439, 1444 (CAFC 1991); *In re Ferens*, 163 USPQ 609).

It is inconceivable as to how the claimed compounds can treat all types of bacterial infections for which applicants provide no competent evidence. For example, there is no common mechanism by which all bacterial infectious conditions arise. Accordingly, treatments for these diseases are normally tailored to the particular type of microorganism or infection present and there is no 'magic bullet' against infections in general. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) due to such infections. The test example in the specification indicates specific types of Gram-positive and Gram-negative organisms (see page 42).

There is no evidence in the record which demonstrates that the screening test relied upon are recognized in the art as being reasonably predictive of success in any of

the contemplated areas of 'therapeutic treatment' of all types of bacterial infections. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse* et al., 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility and not "warranting further study"). The evidence presented in this case does not show such utilities, but only warrants further study.

(Only a few of the references pertinent to the claims are discussed here to make the point of an insufficient disclosure and to indicate that the scope of the claim does not meet the enablement requirement).

1) The nature of the invention: The use of the compound in 'a method of treating bacterial infections' in general.

2) The state of the prior art: There are no known compounds of similar structure that have been demonstrated to be effective against **all** types of bacteria generally.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, 'the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved'. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The online edition of The Merck Manual of Diagnosis and Therapy indicates that 'when bacteremia produces changes in circulation such that tissue perfusion is critically reduced, septic shock ensues' and further provides that 'the

pathogenesis of septic shock is not completely understood'.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: The specification provides tests to determine the activity of the compounds in relation to specific organisms.

6) The breadth of the claims: The instant claims embrace the treatment of 'a disease or disorder due to any type of bacterial infection'.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-21, 23, and 25-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a. In claim 16, the term “acyl” is indefinite. Does this embrace acids of S? P? As? What does the stem look like, i.e. if the acyl is e.g. RC(O), what is R?

b. In claim 16, the phrase "substituted bicyclic carbocyclic or heterocyclic ring system” is not clear. What is covered and what is not? It is recommended that applicants recite specific rings as it is done in claim 17.

Claim Objections

7. Claim 24 is objected to because of the following informalities: In claim 24, the first species at page 11(line 9) the nomenclature “..hydroxy-c-cyclohexanecarboxylic acid” contains a typographical error. The letter “c” in the nomenclature is incorrect. Appropriate correction is required.

8.. Claim 24 is objected to because of the following informalities: The fourth species contains “t-4” and other species at page 11 contain “-r-“ in the nomenclature that appears to be typographical error. Appropriate correction is required.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 16-21, 23, 25-27 and 30-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 and 10-11 of U.S. Patent No. 7,141,564. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is significant overlap between the instant claims 16-21, 23, 25-27 and 30-31 and claims 1-8 and 10-11 of U.S. Patent No. 7,141,564.

11. Claims 16-21, 25-27 and 30-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 9-12 of U.S. Patent No. 6,962,917. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is significant overlap between the instant claims 16-21, 25-27 and 30-31 and claims 1-7 and 9-12 of U.S. Patent No. 6,962,917.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay T. Habte whose telephone number is (571)-272-0667. The examiner can normally be reached on M-F (9.00- 5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kahsay T. Habte/
Primary Examiner, Art Unit 1624

KH
December 16, 2008